

Fig. 9

S-HNC1m

P C G P R G K P G K D G K P G T P G P A	20
GACCCCTGTGGGCCAAGAGGTAAGCCAGGCAAGGATGGAAAACCAGGAACCTCTGGACCAAG	
10 20 30 40 50 60	
G E K G N K G S K G E P I G P A G S D G L	40
CTGGAGAAAAAGGCACAAUAGTCTAAAGGAGAGCCAG GACCAGCTGGATCAGATGGAT	
* 70 80 90 100 110 120	
P C L K G X R G D S G S P A T V T T R G	60
TGCCAGTTCAAAGGAAAACGTTGGAGACAGTGGATCACCT GCAACTGGACAACGAGAG	
130 140 150 160 170 180	
F V F T R H S Q T T A I P S C P E G T V	80
GCTTTGTTTACCCGACACAACTCAAACCAACAGCAATTCTTCATGTCAGAGGGGACAG	
190 200 210 220 230 240	
P L Y S G F S Y L F V Q G N Q R A H G Q	100
TGCCACTCTACAGTGGGTTCTTCTTGTACRAGGAATCAACGAGCCCACGGAC	
250 260 270 280 290 300	
D L G T L G S C L Q R F T T M P F L P C	120
AAGACCTTGAACTCTTGGCAGCTGCTGAGCGATTACACAAATGCCATTCTATTCCT	
310 320 330 340 350 360	
H V N D V C N F A S R N D Y S Y V L S T	140
GCAATGTCATGATGATGATGAAATTTCATGTCAGAAATGATTATCATACTGGCTGTCAA	
370 380 390 400 410 420	
P A L M P H N M A P I T G R A L E P Y I	160
CACCAAGCTCTGATGCCAATGAACATGGCTCCATTACTGGCAGAGCCCTTGAGCCTATA	
430 440 450 460 470 480	
S R C T V C E G P A I A I A V H S Q T T	180
TAAGCAGATGCACTGTTGTGAAGGTCTGGATGCCATAGCCGTTACAGCCAACCA	
490 500 510 520 530 540	
D I F P C P H G V I S L W K G F S F I R	200
CTGACATCTCTGATGCTCAAGGCTGGATTCTCTCTGAAAGGATTTCATTCA	
550 560 570 580 590 600	
T G F R A G S E G T G Q A L X S P G S C L	220
TGTTTCACAAAGTGCAGGTTCTGAGGGCACCGGGCAAGCAGTGGCTCCCTGGCTCTGCC	
510 520 530 540 550 560	
E E F R A S P F L E C H G R G T C R Y Y	240
TGGAAGAAATCCGAGCCAGGCCATTTCTAGAATGTCATGGAAAGGAAACGTGCAACTACT	
610 620 630 640 650 660	
S H S Y S F W L A S L H P E R H F R K P	260
ATTGAAATTCTACAGTTCTGGCTGGCTTCACTAAACCCAGAAAGAATGTTCAAGAACGC	
730 740 750 760 770 780	
I P S T V K A S E L E X I I S R C Q V C	280
CTATTCATCAACTGTGAAAGCTGGGGAAITAGAAAATAAAGTCGCTTCAGGTGT	
790 800 810 820 830 840	
H K K R H *	
GCATGAAGAAAAGACACTGAAGCTAAAAAGACAGCAGAACTGCTATTTCATCCTAA	285
850 860 870 880 890 900	
GAACAAAGTAA	
910	

B-HNC1c

FIG. 2. Nucleotide and derived amino acid sequence of HGA3.3 exons. Bent arrows indicate the 5'- and 3'-borders of each exon and the beginning of the NC1 domain. The RGD sequence is underlined. The boxed amino acid is different from that previously reported (11). Positions of the oligonucleotides S-HNC1m and B-HNC1c used for PCR amplification of a human α 3(IV) cDNA are indicated. Amino Acids 1-67 have not been previously reported (11).

EXHIBIT

3
300

A

tled3

ay, June 17, 1998 12:44 PM

10 20 30 40

GLK GKR GDS GSP ATW TTR GFV FTR HSQ TTA IPS CPE GTV PLY SGF
1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV >

50 60 70 80 90

SFL FVQ GNQ RAH GQD LGT LGS CLQ RFT TMP FLP CNV NDV CNF ASR
1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV >

100 110 120 130

NDY STW LST PAL MPM NMA BIT GRA LEP YIS RCT VCE GPA IAI AVH
1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV >

140 150 160 170 180

SQT TDI PPC PHG WIS LWK GFS FIM FTS AGS EGT GQA LAS PGS CLE
1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV >

190 200 210 220

EFR ASP FLE CHG RGT CNY YSN SYS FWL ASL NPE RMF RKP IPS TVK
1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV >

230 240

AGE LEK IIS RCQ VCM KKR H
1427 TO 1670 OF FU >

Fig. 10

G FIG. 18A

pET22b(+) forward primer

5'-CGGGATCCAGGT TTG AAA GGA AAA CGT-3' (SEQ ID NO:11)

pET22b(+) reverse primer:

5'-CCCAAGCTT TCA GTG TCT TTT CTT CAT-3' (SEQ ID NO:12)

5	10	15	20	25	30	35	40	45
ccg	aat	ttq	aaa	qqa	aaa	cgt	gga	gac
50	55	60	65	70	75	80	85	90
tgg	aca	acg	aga	ggc	ttt	gtc	ttc	acc
95	100	105	110	115	120	125	130	135
gca	att	cct	tca	tgt	cca	gag	ggg	aca
140	145	150	155	160	165	170	175	180
ttt	tct	ttt	ctt	ttt	gta	caa	gga	aat
185	190	195	200	205	210	215	220	225
gac	ctt	gga	act	ctt	ggc	agc	tgc	ctg
230	235	240	245	250	255	260	265	270
cca	ttc	tta	ttc	tgc	aat	gtc	aat	tat
275	280	285	290	295	300	305	310	315
cga	aat	gat	tat	tca	tac	tgg	ctg	atg
320	325	330	335	340	345	350	355	360
atg	aac	atg	gct	ccc	att	act	ggc	aga
365	370	375	380	385	390	395	400	405
agc	aga	tgc	act	gtt	tgt	gaa	ggg	cct
410	415	420	425	430	435	440	445	450
cac	agc	caa	acc	act	gac	att	cct	cca
455	460	465	470	475	480	485	490	495
tct	ctc	tgg	aaa	gga	ttt	tca	ttc	atc
500	505	510	515	520	525	530	535	540
tct	gag	ggc	acc	ggg	caa	gca	ctg	gcc
545	550	555	560	565	570	575	580	585
gaa	gaa	tcc	cga	gcc	agg	tgt	cat	gga
590	595	600	605	610	615	620	625	630
acg	tgc	aac	tac	tat	tca	aat	tcc	tac
635	640	645	650	655	660	665	670	675
tta	aac	cca	gaa	aga	atg	ttc	tgg	ctg
680	685	690	695	700	705	710	715	720
aaa	gct	ggg	gaa	tta	gaa	aaa	ata	ata
725	730	735						
<u>atq aaq aaa aga cac tqa</u> (SEQ ID NO:9)								

pET22b- α 3(IV) NC1 = nucleotides ~~333~~ through ~~735~~ ~~732~~Tumstatin 333 = nucleotides ~~333~~ through ~~375~~ ~~732~~Tumstatin 334 - nucleotide ~~376~~ through ~~735~~ ~~732~~
~~373~~

EXHIBIT

B

FIG. 18B

*
5 10 15 20 25 30 35 40 45
XGL KGK RGD SGS PAT WTT RGF VFT RHS QTT AIP SCP EGT VPL YSG

50 55 60 65 70 75 80 85 90
FSF LFV QGN QRA HGQ DLG TLG SCL QRF TTM PFL FCN VND VCN FAS

95 100 105 110 115 120 125 130 135
RND YSY WLS TPA LMP MNM API TGR ALE PYI SRC TVC EGP AIA IAV

140 145 150 155 160 165 170 175 180
HSQ TTD IPP CPH GWI SLW KGF SFI MFT SAG SEG TGQ ALA SPG SCL

185 190 195 200 205 210 215 220 225
EEF RAS PFL ECH GRG TCN YYF NSY SFW LAS LNP ERM FRK PIP STV

230 235 240 ⁺~~245-244~~
KAG ELE KII SRC QVC MKK RH (SEQ ID NO:10)

pET22b α3(IV) NC1 = residues ¹/ through ~~245-244~~
Tumstatin 333 = residues ¹/ through ~~125-124~~
Tumstatin 334 = residues ¹²⁶ through ~~245-244~~
¹²⁵

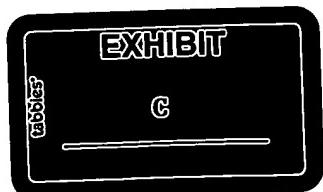


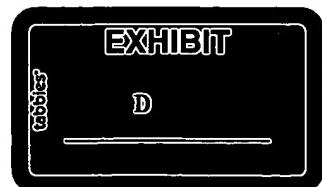
FIG. 42

T1 GP-A
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T2 T3 T4
SGFSFLFVQGNQRRAHGQDLGTLGSCLQRFTTMPFLFCNVNDVC

T3 T5 T6
NFASRNDYSYWLSTPALMPMNMAPITGRALEPYISRCTVCEGP

T6 GP-B
AIAIAVHSQTTDIPPCPHGWISLWKGSFIMFTSAGSEGTGQA
LASPGSCLEEFRASPFLCHGRGTCNYYSNSYSFWLASLNPER
MFRKPIPSTVKAGELEKIIISRCQVCMKKRH



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<120> ANTI-ANGIOGENIC PROTEINS AND FRAGMENTS
AND METHODS OF USE THEREOF

<130> 1440.1027-016

{<140> US 10/032,221
<141> 2001-12-21}

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1	5						10						15				

gac	cca	cag	tgt	cct	tct	ggg	acc	aaa	att	ctt	tac	cac	ggg	tac	tct		96
Asp	Pro	Gln	Cys	Pro	Ser	Gly	Thr	Lys	Ile	Leu	Tyr	His	Gly	Tyr	Ser		
20	25												30				

ttg	ctc	tac	gtg	caa	ggc	aat	gaa	cgg	gcc	cat	gga	cag	gac	ttg	ggc		144
Leu	Leu	Tyr	Val	Gln	Gly	Asn	Glu	Arg	Ala	His	Gly	Gln	Asp	Leu	Gly		
35			40										45				

EXHIBIT

tabbies®

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65 70 75 80	
tac tgg ctg tcc acc cct gag ccc atg ccc atg tca atg gca ccc atc Tyr Trp Leu Ser Thr Pro Glu Pro Met Pro Met Ser Met Ala Pro Ile	288
85 90 95	
acg ggg gaa aac ata aga cca ttt att agt agg tgt gct gtg tgt gag Thr Gly Glu Asn Ile Arg Pro Phe Ile Ser Arg Cys Ala Val Cys Glu	336
100 105 110	
gcg cct gcc atg gtg atg gcc gtg cac agc cag acc att cag atc cca Ala Pro Ala Met Val Met Ala Val His Ser Gln Thr Ile Gln Ile Pro	384
115 120 125	
ccg tgc ccc agc ggg tgg tcc tcg ctg tgg atc ggc tac tct ttt gtg Pro Cys Pro Ser Gly Trp Ser Ser Leu Trp Ile Gly Tyr Ser Phe Val	432
130 135 140	
atg cac acc agc gct ggt gca gaa ggc tct ggc caa gcc ctg gcg tcc Met His Thr Ser Ala Gly Ala Glu Gly Ser Gly Gln Ala Leu Ala Ser	480
145 150 155 160	
ccc ggc tcc tgc ctg gag gag ttt aga agt gcg cca ttc atc gag tgt Pro Gly Ser Cys Leu Glu Glu Phe Arg Ser Ala Pro Phe Ile Glu Cys	528
165 170 175	
cac ggc cgt ggg acc tgc aat tac tac gca aac gct tac agc ttt tgg His Gly Arg Gly Thr Cys Asn Tyr Tyr Ala Asn Ala Tyr Ser Phe Trp	576
180 185 190	
ctc gcc acc ata gag agg agc gag atg ttc aag aag oct acg ccg tcc Leu Ala Thr Ile Glu Arg Ser Glu Met Phe Lys Lys Pro Thr Pro Ser	624
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acc ttg aag gca ggg gag ctg cgc acg cac gtc agc cgc tgc caa gtc Thr Leu Lys Ala Gly Glu Leu Arg Thr His Val Ser Arg Cys Gln Val	672
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 35 40 45
 Thr Ala Gly Ser Cys Leu Arg Lys Phe Ser Thr Met Pro Phe Leu Phe
 50 55 60
 Cys Asn Ile Asn Asn Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser
 65 70 75 80
 Tyr Trp Leu Ser Thr Pro Glu Pro Met Pro Met Ser Met Ala Pro Ile
 85 90 95
 Thr Gly Glu Asn Ile Arg Pro Phe Ile Ser Arg Cys Ala Val Cys Glu
 100 105 110
 Ala Pro Ala Met Val Met Ala Val His Ser Gln Thr Ile Gln Ile Pro
 115 120 125
 Pro Cys Pro Ser Gly Trp Ser Ser Leu Trp Ile Gly Tyr Ser Phe Val
 130 135 140
 Met His Thr Ser Ala Gly Ala Glu Gly Ser Gly Gln Ala Leu Ala Ser
 145 150 155 160
 Pro Gly Ser Cys Leu Glu Glu Phe Arg Ser Ala Pro Phe Ile Glu Cys
 165 170 175
 His Gly Arg Gly Thr Cys Asn Tyr Tyr Ala Asn Ala Tyr Ser Phe Trp
 180 185 190
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 20 25 30
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 50 55 60
 aac cct ggt gat gtc tgc tac tat gcc agc cgg aac gac aag tcc tac Asn Pro Gly Asp Val Cys Tyr Ala Ser Arg Asn Asp Lys Ser Tyr
 65 70 75 80
 tgg ctc tct acc act gcg ccg ctg ccc atg atg ccc gtg gcc gag gac Trp Leu Ser Thr Thr Ala Pro Leu Pro Met Met Pro Val Ala Glu Asp
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 gag atc aag ccc tac atc agc cgc tgt tct gtg tgt gag gcc ccg gcc Glu Ile Lys Pro Tyr Ile Ser Arg Cys Ser Val Cys Glu Ala Pro Ala
 100 105 110
 atc gcc atc gcg gtc cac agt cag gat gtc tcc atc cca cac tgc cca Ile Ala Ile Ala Val His Ser Gln Asp Val Ser Ile Pro His Cys Pro
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 130 135 140
 gcg ggc gga gac gaa ggc ggt ggc caa tca ctg gtg tca ccg ggc agc Ala Ala Gly Asp Glu Gly Gly Gln Ser Leu Val Ser Pro Gly Ser
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 aag gcc ggc ctc atc cgc aca cac atc agc cgc tgc cag gtg tgc atg Lys Ala Gly Leu Ile Arg Thr His Ile Ser Arg Cys Gln Val Cys Met
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 Lys Asn Leu

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Trp Leu Ser Thr Thr Ala Pro Leu Pro Met Met Pro Val Ala Glu Asp
85 90 95
Glu Ile Lys Pro Tyr Ile Ser Arg Cys Ser Val Cys Glu Ala Pro Ala
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Ile Ala Ile Ala Val His Ser Gln Asp Val Ser Ile Pro His Cys Pro
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Ala Gly Trp Arg Ser Leu Trp Ile Gly Tyr Ser Phe Leu Met His Thr
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Cys Leu Glu Asp Phe Arg Ala Thr Pro Phe Ile Glu Cys Asn Gly Gly
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Arg Gly Thr Cys His Tyr Tyr Ala Asn Lys Tyr Ser Phe Trp Leu Thr
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Thr Thr Arg Gly Phe Val Phe Thr Arg His Ser Gln Thr Thr Ala Ile
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Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys
65 70 75 80

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Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr
85 90 95

tgg ctg tca aca cca gct ctg atg cca atg aac atg gct ccc att act 336
Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr
100 105 110

ggc aga gcc ctt gag cct tat ata agc aga tgc act gtt tgt gaa ggt 384
Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly
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Phe Thr Ser Ala Gly Ser Glu Gly Thr Gly Gln Ala Leu Ala Ser Pro
165 170 175

ggc tcc tgc ctg gaa gaa ttc cga gcc agc cca ttt cta gaa tgt cat 576
Gly Ser Cys Leu Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His

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gct tca tta aac cca gaa aga atg ttc aga aag cct att cca tca act Ala Ser Leu Asn Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr 210 215 220			672
gtg aaa gct ggg gaa tta gaa aaa ata ata agt cgc tgt cag gtg tgc Val Lys Ala Gly Glu Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys 225 230 235 240			720
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Arresten

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ttcggaattc tctgttgc acggcttc

28

<210> 16

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<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> pPICZaA reverse oligonucleotide primer for Arresten

<400> 16
tgctctagag gtgttcttct catacagact tggca 35

<210> 17
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> pPICZaA forward oligonucleotide primer for Canstatin

<400> 17
ttcggattc gtcagcatcg gctacacct g 31

<210> 18
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> pPICZaA reverse oligonucleotide primer for Canstatin

<400> 18
gggttacccc caggttcttc atgcacacct gg 32

<210> 19
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> Tumstatin (amino acids 1-244) . Deleted Sequence

<400> 19
Pro Gly Ieu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp
1 5 10 15
Thr Thr Arg Gly Phe Val Phe Thr Arg His Ser Gln Thr Thr Ala Phe
20 25 30
Pro Ser Cys Pro Glu Gly Thr Val Pro Leu Tyr Ser Gly Phe Ser Phe
35 40 45
Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr
50 55 60
Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys
65 70 75 80
Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr
85 90 95
Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr
100 105 110
Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val Cys Gln Gly

115	120	125
Pro Ala Ile Ala Ile Ala Val His Ser Gln Thr Thr Asp Ile Pro Pro		
130	135	140
Cys Pro His Gly Trp Ile Ser Leu Trp Lys Gly Phe Ser Phe Ile Met		
145	150	155
Phe Thr Ser Ala Gly Ser Glu Gly Thr Gly Gln Ala Leu Ala Ser Pro		
165	170	175
Gly Ser Cys Leu Glu Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His		
180	185	190
Gly Arg Gly Thr Cys Asn Tyr Tyr Ser Asn Ser Tyr Ser Phe Trp Leu		
195	200	205
Ala Ser Leu Asn Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr		
210	215	220
Val Lys Ala Gly Glu Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys		
225	230	235
Met Lys Lys Arg		240

<210> 20
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Tumstatin 333 (amino acids 1-125 of SEQ ID NO:10)

<400> 20
Gly Leu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp Thr
1 5 10 15
Thr Arg Gly Phe Val Phe Thr Arg His Ser Gln Thr Thr Ala Ile Pro
20 25 30
Ser Cys Pro Glu Gly Thr Val Pro Leu Tyr Ser Gly Phe Ser Phe Leu
35 40 45
Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr Leu
50 55 60
Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys Asn
65 70 75 80
Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr Trp
85 90 95
Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr Gly
100 105 110
Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val
115 120

<210> 21
<211> 119-120
<212> PRT
<213> Artificial Sequence

<220>
<223> Tumstatin 334 (amino acids 126-244 of SEQ ID NO:10)

<400> 21
Cys Glu Gly Pro Ala Ile Ala Ile Val His Ser Gln Thr Thr Asp
1 5 10 15
Ile Pro Pro Cys Pro His Gly Trp Ile Ser Leu Trp Lys Gly Phe Ser

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20 25 30
Phe Ile Met Phe Thr Ser Ala Gly Ser Glu Gly Thr Gly Gln Ala Leu
35 40 45
Ala Ser Pro Gly Ser Cys Leu Glu Glu Phe Arg Ala Ser Pro Phe Leu
50 55 60
Glu Cys His Gly Arg Gly Thr Cys Asn Tyr Tyr Ser Asn Ser Tyr Ser
65 70 75 80
Phe Trp Leu Ala Ser Leu Asn Pro Glu Arg Met Phe Arg Lys Pro Ile
85 90 95
Pro Ser Thr Val Lys Ala Gly Glu Leu Glu Lys Ile Ile Ser Arg Cys
100 105 110
Gln Val Cys Met Lys Lys Arg His
115

<210> 22
<211> 191
<212> PRT
<213> Artificial Sequence

<220>
<223> Tum-1 (Tumstatin N53) (amino acids 54-244 of SEQ
ID NO:10)

<400> 22
~~Asn~~ Gln Arg Ala His Gly Gln Asp Leu Gly Thr Leu Gly Ser Cys Leu
1 5 10 15
Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys Asn Val Asn Asp Val
20 25 30
Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr Trp Leu Ser Thr Pro
35 40 45
Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr Gly Arg Ala Leu Glu
50 55 60
Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly Pro Ala Ile Ala Ile
65 70 75 80
Ala Val His Ser Gln Thr Thr Asp Ile Pro Pro Cys Pro His Gly Trp
85 90 95
Ile Ser Leu Trp Lys Gly Phe Ser Phe Ile Met Phe Thr Ser Ala Gly
100 105 110
Ser Glu Gly Thr Gly Gln Ala Leu Ala Ser Pro Gly Ser Cys Leu Glu
115 120 125
Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His Gly Arg Gly Thr Cys
130 135 140
Asn Tyr Tyr Ser Asn Ser Tyr Ser Phe Trp Leu Ala Ser Leu Asn Pro
145 150 155 160
Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr Val Lys Ala Gly Glu
165 170 175
Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys Met Lys Lys Arg His
180 185 190

<210> 23
<211> 132
<212> PRT
<213> Artificial Sequence

<220>
<223> Tum-2 (amino acids 1-132 of SEQ ID NO:10)

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<400> 23
~~Phe~~ Gly Leu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp
1 5 10 15
Thr Thr Arg Gly Phe Val Phe Thr Arg His Ser Gln Thr Thr Ala Ile
20 25 30
Pro Ser Cys Pro Glu Gly Thr Val Pro Leu Tyr Ser Gly Phe Ser Phe
35 40 45
Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr
50 55 60
Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys
65 70 75 80
Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr
85 90 95
Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr
100 105 110
Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly
115 120 125
Pro Ala Ile Ala *Ile*
130

<210> 24
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Tum-3 (amino acids 133-244 of SEQ ID NO:10)

<400> 24
~~Ile~~ Ala Val His Ser Gln Thr Thr Asp Ile Pro Pro Cys Pro His Gly
1 5 10 15
Trp Ile Ser Leu Trp Lys Gly Phe Ser Phe Ile Met Phe Thr Ser Ala
20 25 30
Gly Ser Glu Gly Thr Gly Gln Ala Leu Ala Ser Pro Gly Ser Cys Leu
35 40 45
Glu Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His Gly Arg Gly Thr
50 55 60
Cys Asn Tyr Tyr Ser Asn Ser Tyr Ser Phe Trp Leu Ala Ser Leu Asn
65 70 75 80
Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr Val Lys Ala Gly
85 90 95
Glu Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys Met Lys Lys Arg *H's*
100 105 110

<210> 25
<211> 64
<212> PRT
<213> Artificial Sequence

<220>
<223> Tum-4 (amino acids 181-244 of SEQ ID NO:10)

<400> 25
~~Glu~~ Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His Gly Arg Gly Thr
1 5 10 15
Cys Asn Tyr Tyr Ser Asn Ser Tyr Ser Phe Trp Leu Ala Ser Leu Asn
20 25 30

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Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr Val Lys Ala Gly
35 40 45
Glu Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys Met Lys Lys Arg H's
50 55 60

<210> 26
<211> 79
<212> PRT
<213> Artificial Sequence

<220>
<223> Tum-5 (amino acids 54-132 of SEQ ID NO:10)

<400> 26
~~Asn~~ Gln Arg Ala His Gly Gln Asp Leu Gly Thr Leu Gly Ser Cys Leu
1 5 10 15
Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys Asn Val Asn Asp Val
20 25 30
Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr Trp Leu Ser Thr Pro
35 40 45
Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr Gly Arg Ala Leu Glu
50 55 60
Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly Pro Ala Ile Ala *Ile*
65 70 75

<210> 27
~~20~~ 19
<212> PRT
<213> Artificial Sequence

<220>
<223> T1 (amino acids 1-~~20~~ 19 of SEQ ID NO:10)

<400> 27
~~Pro~~ Gly Leu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp
1 5 10 15
Thr Thr Arg Gly
20

<210> 28
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> T2 (amino acids ~~54-73~~ 53-72 of SEQ ID NO:10)

<400> 28
Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr Leu Gly Ser Cys Leu
1 5 10 15
Gln Arg Phe Thr
20

<210> 29
<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> T3 (amino acids ~~69-86~~⁶⁸⁻⁸⁷ of SEQ ID NO:10)

<400> 29

Leu	Gln	Arg	Phe	Thr	Thr	Met	Pro	Phe	Leu	Phe	Cys	Asn	Val	Asn	Asp
1				5					10					15	
Val	Cys	Asn	Phe												20

<210> 30

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> T4 (amino acids ~~84-103~~⁸³⁻¹⁰² of SEQ ID NO:10)

<400> 30

Asp	Val	Cys	Asn	Phe	Ala	Ser	Arg	Asn	Asp	Tyr	Ser	Tyr	Trp	Leu	Ser
1					5					10				15	
Thr	Pro	Ala	Leu												20

<210> 31

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> T5 (amino acids ~~95-117~~⁹⁸⁻¹¹⁶ of SEQ ID NO:10)

<400> 31

Ser	Thr	Pro	Ala	Leu	Met	Pro	Met	Asn	Met	Ala	Pro	Ile	Thr	Gly	Arg
1					5					10				15	
Ala	Leu	Glu													

<210> 32

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> T6 (amino acids ~~114-122~~¹¹³⁻¹³¹ of SEQ ID NO:10)

<400> 32

Arg	Ala	Leu	Glu	Pro	Tyr	Ile	Ser	Arg	Cys	Thr	Val	Cys	Glu	Gly	Pro
1					5					10			15		
Ala	Ile	Ala													

<210> 33

<211> 88
<212> PRT
<213> Artificial Sequence

<220>
<223> Tumstatin-45-132 (amino acids 45-132 of SEQ ID NO:10)

<400> 33
~~Gly~~ Phe Ser Phe Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln
1 5 10 15
Asp Leu Gly Thr Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro
20 25 30
Phe Leu Phe Cys Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn
35 40 45
Asp Tyr Ser Tyr Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met
50 55 60
Ala Pro Ile Thr Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr
65 70 75 80
Val Cys Glu Gly Pro Ala Ile Ala *Ile*
85

<210> 34
<211> 88
<212> PRT
<213> Artificial Sequence

<220>
<223> Tumstatin-5-~~126~~¹²⁵-C-A (amino acids 45-132 of SEQ ID NO:10; alanine has been substituted for the cysteine residue at position ~~126~~¹²⁵ of the full-length Tumstatin molecule)~~us~~

<400> 34
~~Gly~~ Phe Ser Phe Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln
1 5 10 15
Asp Leu Gly Thr Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro
20 25 30
Phe Leu Phe Cys Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn
35 40 45
Asp Tyr Ser Tyr Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met
50 55 60
Ala Pro Ile Thr Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr
65 70 75 80
Val Ala Glu Gly Pro Ala Ile Ala *Ile*
85

<210> 35
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic blocking peptide

<400> 35
Cys Asp Cys Arg Gly Asp Cys Phe Cys

1 5

<210> 36
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic blocking peptide

<400> 36
Cys Asn Gly Arg Cys
1 5

<210> 37
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> T7 (amino acids ⁷³⁻⁹⁷ ~~74-98~~ of SEQ ID NO:10)

<400> 37
Thr Met Pro Phe Leu Phe Cys Asn Val Asn Asp Val Cys Asn Phe Ala
1 5 10 15
Ser Arg Asn Asp Tyr Ser Tyr Trp Leu
20 25

<210> 38
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> T7-mutant (amino acids ⁷³⁻⁹⁷ ~~74-98~~ of SEQ ID NO:10;
methionine has been substituted for the leucine
residue at position ⁷⁷ ~~74~~ of the full-length
Tumstatin molecule, and isoleucine has been
substituted for valine at position ⁸¹ ~~82~~, and
asparagine has been substituted for aspartic acid
at position ⁸⁴ ~~83~~)

<400> 38
Thr Met Pro Phe Met Phe Cys Asn Ile Asn Asn Val Cys Asn Phe Ala
1 5 10 15
Ser Arg Asn Asp Tyr Ser Tyr Trp Leu
20 25

<210> 39
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> T8 (amino acids ⁹⁶⁸⁻⁹⁴ ~~69-95~~ of SEQ ID NO:10; lysine has

been substituted for the leucine residue at
position ~~68~~⁶⁹ of the full-length Tumstatin molecule)

<400> 39
 Lys Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys Asn Val Asn Asp
 1 5 10 15
 Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser
 20 25

<210> 40

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> T8-3 (amino acids ~~69-95~~^{68 94} of SEQ ID NO:10; lysine
has been substituted for the leucine residue at
position ~~69~~⁷⁰ of the full-length Tumstatin molecule,
and serine has been substituted for the cysteine
residues at positions ~~80~~⁷⁹ and ~~86~~⁸⁵)

<400> 40

Lys Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Ser Asn Val Asn Asp
 1 5 10 15.
 Val Ser Asn Phe Ala Ser Arg Asn Asp Tyr Ser
 20 25

<210> 41

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> TP3 (amino acids ~~77-95~~^{76 94} of SEQ ID NO:10; lysine has
been substituted for the phenylalanine residue at
position ~~77~~⁷⁸ of the full-length Tumstatin molecule,
and cysteine has been substituted for the aspartic
acid at position ~~84~~⁸³)

<400> 41

Lys Leu Phe Cys Asn Val Asn Cys Val Cys Asn Phe Ala Ser Arg Asn
 1 5 10 15
 Asp Tyr Ser

<210> 42

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> P2 (amino acids ~~69-95~~^{68 94} of SEQ ID NO:10; lysine has
been substituted for the leucine residue at
position ~~69~~⁷⁰ of the full-length Tumstatin molecule,
and aspartic acid has been substituted for the
cysteine residues at positions ~~80~~⁷⁹ and ~~86~~⁸⁵)

<400> 42
 Lys Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Asp Asn Val Asn Asp
 1 5 10 15
 Val Asp Asn Phe Ala Ser Arg Asn Asp Tyr Ser
 20 25

<210> 43
 <211> 27
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Scrambled peptide SP1

<400> 43
 Ala Asn Met Ser Arg Asn Val Phe Phe Asp Cys Thr Ser Phe Pro Val
 1 5 10 15
 Cys Gln Lys Phe Leu Asn Asp Thr Arg Asn Tyr
 20 25

<210> 44
 <211> 27
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Scrambled peptide SP2

<400> 44
 Thr Phe Asn Cys Val Lys Asn Tyr Gln Arg Leu Asp Phe Thr Ser Arg
 1 5 10 15
 Phe Val Met Asp Ser Cys Ala Asn Phe Pro Asn
 20 25

<210> 45
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Generic peptide

<223> X at position 1 is a ~~hydrogen or a peptidyl chain~~
~~of 1 to 17 amino acids~~
 any amino acid
 <223> X at position 2 is F or K
 phe lys
 <223> X at position 5 is C, S or D
 cys ser asp
 <223> X at position 9 is D or C
 asp cys
 <223> X at position 11 is C, S or D
 cys ser asp
 <223> X at position 14 is a ~~hydrogen or a peptidyl chain~~
~~of 1 to 12 amino acids~~
 any amino acid

<400> 45
Xaa Xaa Leu Phe Xaa Asn Val Asn Xaa Val Xaa Asn Phe Xaa
1 5 10

<210> 46
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 46
Thr Thr Met Pro
1

<210> 47
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 47
Phe Thr Thr Met Pro
1 5

<210> 48
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 48
Arg Phe Thr Thr Met Pro
1 5

<210> 49
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 49
Gln Arg Phe Thr Thr Met Pro
1 5

<210> 50
<211> 8

<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 50
Leu Gln Arg Phe Thr Thr Met Pro
1 5

<210> 51
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 51
Lys Gln Arg Phe Thr Thr Met Pro
1 5

<210> 52
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 52
Ala Ser Arg Asn
1

<210> 53
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 53
Ala Ser Arg Asn Asp
1 5

<210> 54
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 54

Ala Ser Arg Asn Asp Tyr
1 5

<210> 55
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 55
Ala Ser Arg Asn Asp Tyr Ser
1 5

<210> 56
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 56
Ala Ser Arg Asn Asp Tyr Ser Tyr
1 5

<210> 57
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 57
Ala Ser Arg Asn Asp Tyr Asp Tyr Trp
1 5

<210> 58
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 58
Ala Ser Arg Asn Asp Tyr Ser Tyr Trp Leu
1 5 10